In the Specification

On page 37, line 29, before the semicolon, insert the following --who describe how scientists design drugs using powerful computer-graphics hardware and software by first inputting the coordinates or positions of the atoms of the structure of the protein to be inhibited into the computer, determining the structure and orientation of the natural ligand that binds to an active site of the protein, and introducing appropriate chemical groups onto this framework to design a molecule that should interact with the amino acids lining the walls of the active site of the protein to cause the desired effect (in particular, the design of drugs inhibiting phospholipase A_2 and haemoglobin are described)--.

On page 37, line 30, before the semicolon, insert the following --who describe rational antiviral drug design, defined as the directed synthesis of new compounds based on an understanding of a prototype drug/viral structural or functional protein interaction at the atomic level, and, in particular, describe the use of supercomputers and new computational approaches to permit consideration of previously impossible computational problems such as the use of thermodynamic calculations, such as the thermodynamic-cyclic perturbation approach, which enables one to calculate the relative free energy change for the binding of two different compounds and enables the

researcher to predict whether a compound proposed for synthesis is likely to possess a greater binding affinity to the target, and the molecular dynamics simulations approach, which simulate the dynamics of the drug/protein interactions based on the dynamical trajectories of each atom to help identify areas of the drug where considerable movement is occurring when bound to the target, suggesting that the conformation of the drug may need to be constrained to maximize activity and suggesting ways in which the drug is exerting its effect on the protein--.

On page 37, line 32, before the semicolon, insert the following --who describe the use of three-dimensional modelling databases for identifying structure activity relationships and, in particular, describe the ChemStat™ database (available from Chemical Design Ltd., Oxford, England), a module of the molecular modelling software Chem-X (also available from Chemical Design Ltd., Oxford, England), containing molecular coordinates with computed and experimental parameters and biological data for computerized drug design--.

On page 37, line 33, before the semicolon, insert the following --who describe the brute force techniques, subgraph addition, and spacer skeletons approaches to obtaining molecular graphs that span specified binding sites and incorporate predicted ligand points at their vertices for drug design (spacer skeletons are assemblies of molecular subgraphs and are used to

reduce the combinatorial problems of structure generation to a practicable level for future analysis); assemblies of rings are examined for planarity by searching the Cambridge Structural Database, The Cambridge Crystallographic Data Centre, Cambridge, England, which is used to find all the compounds that contain a certain molecular fragment and to calculate the geometric parameters of this fragment in each compound; use of the GEOM program, the PLUTO 78 package, and the GENOA program for drug design are also discussed--.

On page 37, line 35, before the period, insert the following --who describe synthetic and structural experiments for the characterization of a new class of model receptors for adenine derivatives in which systemic structural modifications in both cyclohexyluracil and 9-ethyladenine revealed trends concerning steric effects and acid-base effects. The model systems were used to examine the kinetics of the base-pairing event. In this paper, Askew et al. describe that their departure from previous model studies was made possible by the construction of a new molecular shape that permits both hydrogen bonding and aromatic stacking forces to act simultaneously. The structural developments were a consequence of the use of Kemp's triacid, in which a U-shaped (diaxial) relationship exists between any two carboxyl functions. Conversion of the triacid to the imide acid chloride gave an acylating agent that could be attached via amide

or ester linkages to practically any available aromatic surface. The resulting structure features an aromatic plane which can be roughly parallel to that of the atoms in the imide function; hydrogen bonding and stacking forces converge from perpendicular directions to provide a microenvironment complimentary to adenine derivatives--.

On page 39, lines 27-28, please delete, without prejudice, the words "are specifically incorporated by reference. Other" and insert therein the words --and other--.

On page 40, delete lines 1-2.

In the Claims

7. (Amended) The method of claim 1 wherein the critical region of the targeted ribonucleic acid is determined by mutation of regions of the targeted RNA and analysis of the [amino acid sequence derived from] function of the mutated RNA.

REMARKS

The present application is directed to a method and compounds for inhibiting RNA function. Compounds are designed that bind to nucleotides exposed on the surface of the minor groove of the targeted RNA molecules. The presence of the compound within the minor groove inhibits RNA function.

Applicant notes that Claim 7 has been amended to clarify that the critical region of the target RNA is determined by